

## PATENT COOPERATION TREATY

**PCT**



REC'D 18 JAN 2005

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**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**  
(PCT Article 36 and Rule 70)

Applicant's or agent's file reference R2554-PCT	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/EP 03/10715	International filing date (day/month/year) 24.09.2003	Priority date (day/month/year) 30.09.2002
International Patent Classification (IPC) or both national classification and IPC A61K9/00		
Applicant UNIVERSITEIT GENT et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets, including this cover sheet.  <input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).  These annexes consist of a total of 1 sheets.
3. This report contains indications relating to the following items:  I <input checked="" type="checkbox"/> Basis of the opinion II <input type="checkbox"/> Priority III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application

Date of submission of the demand  16.04.2004	Date of completion of this report  17.01.2005
Name and mailing address of the International preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer  Villa Riva, A  Telephone No. +49 89 2399-8404  

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/10715

## I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*):

### Description, Pages

1-27 as originally filed

### Claims, Numbers

6-18 as originally filed

1-5 received on 03.05.2004 with letter of 03.05.2004

### Drawings, Sheets

1/4-4/4 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

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EXAMINATION REPORT**

International application No. **PCT/EP 03/10715**

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5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-18
	No: Claims	
Inventive step (IS)	Yes: Claims	1-18
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-18
	No: Claims	

2. Citations and explanations

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement**

Reference is made to the following documents:

- D1 - WO 99/63971 A , disclosing preparations with a microosmotic core, optionally coated for the controlled delivery of drugs.
- D2 - WO 99/51208 A , disclosing a matrix with controlled erosion
- D3 - WO 89/09066 A, disclosing preparations comprising a matrix with controlled erosion, optionally coated
- D4 - US 5 213 808 A , disclosing multilayered pharmaceutical forms with a matrix and surfactant;
- D5 WO 01/05376 A, disclosing felodipine pharmaceutical forms with a matrix and a "solubilizer"

Unless otherwise indicated, reference is made to the relevant passages emphasized in the International Search Report.

In several of the cited prior art items (D1, D2, D6), preparations with the same or a very similar structure and the same ingredients are disclosed. They also can be optionally coated. However, in all cases, the hydrophilic cellulose polymer is present in the core in a quantity which is greater than that of the amphiphilic material.

Therefore novelty is acknowledged to the present set of claims. In view of the good in vitro and in vivo results, the presence of an inventive step can be acknowledged as well.

In summary, present claims 1-18 appear to comply with the requirements of the PCT as far as novelty, inventivity and industrial applicability are concerned.

CLAIMS

(96)

1. A biologically active composite solid shaped article comprising an outer layer and an inner core, wherein:

(a) the outer layer is an extrudable coating retaining the structural integrity of the inner core and consisting of :

- at least one polymeric component selected from the group consisting of hydrophobic cellulose polymers, acrylate (co)polymers, polyvinylpyrrolidone, polyethylene oxide, polyvinyl alcohol, poly(ethylene-co-vinyl acetate), and
- optionally at least one plasticizer for the said polymeric component,

(b) the inner core fills said outer layer and comprises:

- at least a biologically active ingredient, and
- an excipient for the said biologically active ingredient, said excipient comprising at least one hydrophilic cellulose polymer and an amphiphilic material, wherein the weight ratio of said hydrophilic cellulose polymer to said amphiphilic material is from 0.2 : 1 to 0.6 : 1.

2. A biologically active composite solid shaped article according to claim 1, wherein the hydrophilic cellulose polymer of the inner core is a hydroxyalkylalkylcellulose.

3. A biologically active composite solid shaped article according to claim 1 or claim 2, wherein the hydrophilic cellulose polymer of the inner core is hydroxypropylmethylcellulose.

4. A biologically active composite solid shaped article according to any of claims 1 to 3, wherein the amphiphilic material of the inner core has both a portion derived from a glyceride and a portion derived from a polyethylene glycol ester.

5. A biologically active composite solid shaped article according to any of claims 1 to 4, wherein the weight ratio of the hydrophilic cellulose polymer to the amphiphilic material in the blend of the inner core is from 0.3 : 1 to 0.6 : 1.

Sheet No. ...1....

**Box No. VIII (iv) DECLARATION: INVENTORSHIP** (only for the purposes of the designation of the United States of America)  
*The declaration must conform to the following standardized wording provided for in Section 214; see Notes to Boxes Nos. VIII, VIII (i) to (v) (in general) and the specific Notes to Box No. VIII (iv). If this Box is not used, this sheet should not be included in the request.*

**Declaration of inventorship (Rules 4.17(iv) and 51bis.1(a)(iv))  
 for the purposes of the designation of the United States of America:**

I hereby declare that I believe I am the original, first and sole (if only one inventor is listed below) or joint (if more than one inventor is listed below) inventor of the subject matter which is claimed and for which a patent is sought.

This declaration is directed to the international application of which it forms a part (if filing declaration with application).

This declaration is directed to international application No. PCT/EP.03/10715..... (if furnishing declaration pursuant to Rule 26ter).

I hereby declare that my residence, mailing address, and citizenship are as stated next to my name.

I hereby state that I have reviewed and understand the contents of the above-identified international application, including the claims of said application. I have identified in the request of said application, in compliance with PCT Rule 4.10, any claim to foreign priority, and I have identified below, under the heading "Prior Applications," by application number, country or Member of the World Trade Organization, day, month and year of filing, any application for a patent or inventor's certificate filed in a country other than the United States of America, including any PCT international application designating at least one country other than the United States of America, having a filing date before that of the application on which foreign priority is claimed.

Prior Applications: GB.0222612.4 .....

I hereby acknowledge the duty to disclose information that is known by me to be material to patentability as defined by 37 C.F.R. § 1.56, including for continuation-in-part applications, material information which became available between the filing date of the prior application and the PCT international filing date of the continuation-in-part application.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Name: Jean Paul Remon .....

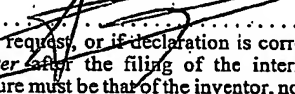
Residence: Melle, Belgium .....

(city and either US state, if applicable, or country)

Mailing Address: J. Youngstraat 14 .....

B-9090 Melle .....

Citizenship: Belgian .....

Inventor's Signature:  .....

(if not contained in the request, or if declaration is corrected or added under Rule 26ter after the filing of the international application. The signature must be that of the inventor, not that of the agent)

Date: October 17<sup>th</sup> 2003 .....

(of signature which is not contained in the request, or of the declaration that is corrected or added under Rule 26ter after the filing of the international application)

Name: Els Mehuys .....

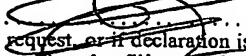
Residence: St.-Denijs Westrem, Belgium .....

(city and either US state, if applicable, or country)

Mailing Address: Putkapelstraat 47 .....

B-9051 St.-Denijs Westrem .....

Citizenship: Belgian .....

Inventor's Signature:  .....

(if not contained in the request, or if declaration is corrected or added under Rule 26ter after the filing of the international application. The signature must be that of the inventor, not that of the agent)

Date: October 17<sup>th</sup> 2003 .....

(of signature which is not contained in the request, or of the declaration that is corrected or added under Rule 26ter after the filing of the international application)

☐ This declaration is continued on the following sheet, "Continuation of Box No. VIII (iv)".

Sheet No: ... 2 ...

Continuation of Box No. VIII (i) to (v) **DECLARATION**

*If the space is insufficient in any of Boxes Nos. VIII (i) to (v) to furnish all the information, including in the case where more than two inventors are to be named in Box No. VIII (iv), in such case, write "Continuation of Box No. VIII..." (indicate the item number of the Box) and furnish the information in the same manner as required for the purposes of the Box in which the space was insufficient. If additional space is needed in respect of two or more declarations, a separate continuation box must be used for each such declaration. If this Box is not used, this sheet should not be included in the request.*

## Continuation of Box No. VIII (iv):

Name: Chris Vervaeet


Residence: Izegem, Belgium

(city and either US state, if applicable, or country)

Mailing Address: Pieter Prulmstraat 11

B-8870 Izegem

Citizenship: Belgian

Inventor's Signature:   
(if not contained in the request, or if declaration is corrected or added under Rule 26ter after the filing of the international application. The signature must be that of the inventor, not that of the agent)

Date: 19 Feb 2003  
(of signature which is not contained in the request, or of the declaration that is corrected or added under Rule 26ter after the filing of the international application)